

Kinetics of Channelized Membrane Ions in Magnetic Fields

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The cyclotron resonance model for channel ion transport in weak magnetic fields is extended to include damping losses. The conductivity tensor is obtained for different electric field configurations, including the circuital field E_ϕ normal to the channel axis. The conductivity behavior close to the cyclotron resonance frequency ω_c is compared to existing Ca^{2+} -efflux data in the literature. A collision time of .023 s results from this comparison under the assumption that K^+ ions are transiting in a 0.35 G field. We estimate a mean kinetic energy of 3.5 eV for this ion at resonance. This model leads to discrete modes of vibration (eigenfrequencies) in the ion-lattice interaction, such that $\omega_n = n\omega_c$. The presence of such harmonics is compatible with recent results by Blackman et al. [1985b] and McLeod et al. [1986] with the interesting exception that even modes do not appear in their observations, whereas the present model has no restriction on n . This harmonic formalism is also consistent with another reported phenomenon, that of quantized multiple conductances in single patch-clamped channels.

Key words: cyclotron resonance, ion channels, multiple conductance, calcium efflux, eigenfrequencies, membrane transport

INTRODUCTION

It is now well established [Hille, 1984; Van Driessche and Zeiske, 1985] that ions can be transported through cell membranes via conduits referred to as pores or (more usually) channels. Channels are structures formed by specialized proteins that span the membrane with certain fascinating regularities. They exhibit near-cylindrical symmetry normal to the plane of the membrane, with the axial direction acting as a sort of wrapping template for the α -helical subunits of the protein body. The possibility exists that this configuration represents a generalized class of structures, all embodying a common physical mechanism controlling charge transport in membranes [Unwin, 1986]. At the same time the growing literature on this subject makes it clear that there are also important differences among channels, e.g., size, ionic selectivity, and energy transduction mechanisms. Schematically we can imagine a channel composed of three connected parts, as indicated in Figure 1A. There is a middle region containing, in the simplest configuration, a tubular channel that extends through the entire membrane thickness ($\sim 40 \text{ \AA}$). There are also two rather specialized geometries at either end, extending away from the membrane and into the cell interior and the

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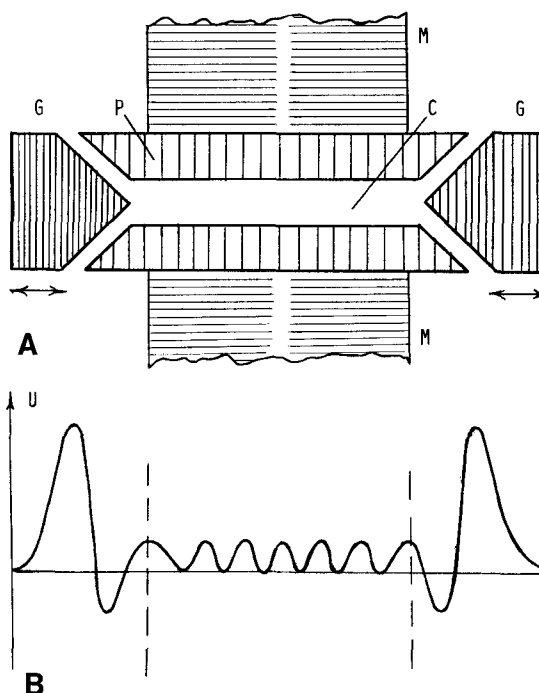


Fig. 1. **A:** Highly schematic representation of an idealized ion channel. The protein P has its axis lying transverse to the membrane M, forming a tubular channel C. Passage is controlled by gates G at either end. **B:** The potential energy U along the axis of such a channel. There are two distinct energy areas: one at either end, connected to the gating mechanism, and another, lower energy region within the channel itself.

extracellular region, for distances equal to or even larger than the membrane thickness. These two end geometries serve as gating mechanisms, allowing influx of ions to the channel at one end and efflux from the channel at the other. The ends of the protein can serve widely varying functions other than admittance or release gates for ions: they can serve as energy transduction sites, as gap junction connectors between cells, and in their most widely recognized role, as receptors for immunological signals or other messages.

An idealized potential energy variation that might be expected [Jordan, 1984; Schmidt and Korzeniewski, 1984] along the axis of such a protein is sketched in Figure 1B. The large potential barriers at either end represent not only the effect of the gates but also the possibility of energetically unfavorable transition states between the completely hydrated and the ligand-associated states of the ion. The binding sites between the ends are at some depth such that, once the barrier energy is overcome, the ion requires much less energy to traverse the channel per s. It is also likely that the potential distribution in this middle area enjoys a periodicity reflecting the repeat order of the internal lattice due to the wraparound α -helices that form the channel. In a number of membrane proteins, these α -helices act as building blocks, twisting together to form either a central cylindrical hole or one that is perhaps interwoven through the body of the protein. Two such examples are the acetylcholine receptor [Popot and Changeux, 1984] and bacteriorhodopsin [Henderson and Unwin, 1975], a

non-mammalian protein that acts as a photon-energized proton pump. It is known that there are channels that are sharply voltage sensitive [Hille, 1984], providing evidence that at least some channel gates can be electrically controlled.

When seeking possible interaction sites to explain the effects of low-frequency electromagnetic fields acting on cellular systems [Goodman et al., 1983; Liboff et al., 1984], the ion channel exhibits interesting properties well suited to such coupling mechanisms. The ionic flow through these channels is responsible for many things, not the least of which is the well-being of the cell, or at least its future state. It is therefore reasonable to expect that perturbation in ion transport can result in altered biological responses. The unidirectional ionic transport in a given channel constitutes a well-defined current. It follows that for cells in electromagnetic fields there may be a basis for a Lorentz-type coupling at each channel, which could conceivably interfere with those critical cell functions governed by membrane transport.

We are also intrigued with the concept that the ionic motion occurring in channels may reflect a set of highly regular constraints imposed by the protein α -helical array. At least two other groups [Kim and Clementi, 1988; Skerra and Brickmann, 1987] recently have argued, using computational molecular dynamics approaches, that various ions moving through gramicidin A channels will follow prescribed helical paths. Earlier it was pointed out [Liboff, 1985] that if transport ions are constrained by the membrane protein channel structure to follow helical paths, then magnetic field coupling to ionic currents may result in a set of gyrofrequencies for the channel system, this set of frequencies corresponding to different cyclotron resonance conditions. The dynamics of charged particles in such systems was explored by McLeod and Liboff [1986] for the case of no damping. In the following section we study this type of coupling in greater detail, concentrating on the kinetic energy of a particle in resonance and, in particular, on the damping losses attached to this motion.

CYCLOTRON RESONANCE CONDUCTIVITY

We [McLeod and Liboff, 1986] previously examined the motion of a charged particle under the influence of a periodic electric field $\mathbf{E}$ and a static field $\mathbf{B}$, obtaining the rectangular velocity components and the kinetic energy as a function of the cyclotron frequency

$$\omega_c = \frac{q}{m} B_o \quad (1)$$

In order to consider the effects of damping on the energy, it is necessary to introduce a relaxation time τ equivalent to the mean time between collisions for a given carrier in a specific milieu. Recall that the undamped force equation is

$$\mathbf{F} = m \frac{d\mathbf{u}}{dt} = q\mathbf{E} + q (\mathbf{u} \times \mathbf{B}) \quad (2)$$

where $\mathbf{u}$ is the particle velocity, q is its charge, and m is its mass. This equation can be rewritten to include the effects of collisions by specifying a damping force

$$\mathbf{R} = b\mathbf{u} \simeq \frac{m\mathbf{u}}{\tau} \quad (3)$$

The force equation then becomes

$$m \frac{d\mathbf{u}}{dt} = q\mathbf{E} + q(\mathbf{u} \times \mathbf{B}) - \frac{m\mathbf{u}}{\tau} \quad (4)$$

If we assume that the velocity is a harmonic function, Equation 4 becomes

$$\frac{\mathbf{u}}{\tau} (1 + i\omega\tau) - \mathbf{u} \times \frac{q}{m} \mathbf{B} = \frac{q}{m} \mathbf{E} \quad (5)$$

Instead of considering only one particle, generalize this to η identical particles in unit volume, each carrying a charge q . If this ensemble moves at a mean velocity $\mathbf{u}$, the current density is

$$\mathbf{J} = \eta q \mathbf{u} = \rho \mathbf{u} \quad (6)$$

where ρ is the charge density. Let B_o be the z -component of $\mathbf{B}$. Multiply Equation 5 by ρ , and make the substitutions

$$\omega_D = \frac{1}{\tau} (1 + i\omega\tau) \quad (7)$$

$$\omega_c = \frac{q}{m} B_o \quad (8)$$

$$\omega_x = \frac{q}{m} B_x \quad (9)$$

$$\omega_y = \frac{q}{m} B_y \quad (10)$$

We then have

$$\omega_D J_x - \omega_c J_y + \omega_y J_z = \rho \frac{q}{m} E_x \quad (11)$$

$$\omega_c J_x + \omega_D J_y - \omega_x J_z = \rho \frac{q}{m} E_y \quad (12)$$

$$-\omega_y J_x + \omega_x J_y + \omega_D J_z = \rho \frac{q}{m} E_z \quad (13)$$

This has the tensor form

$$\bar{\bar{\Omega}} \cdot \mathbf{J} = \rho \left(\frac{q}{m} \right) \mathbf{E} \quad (14)$$

which can be rewritten in terms of the conductivity tensor $\bar{\bar{\sigma}}$.

$$\mathbf{J} = \bar{\bar{\sigma}} \mathbf{E} \quad (15)$$

where

$$\bar{\bar{\sigma}} = \rho \left(\frac{q}{m} \right) \bar{\bar{\Omega}}^{-1} \quad (16)$$

Although determining the nine elements in Equation 16 is straightforward, a considerable reduction in algebra is obtained by restricting the magnetic field to one direction. It is convenient to choose this direction to coincide with the axis of an idealized cylindrical channel, such that $\mathbf{B} = B_o \hat{\mathbf{z}}$. The elements of Equation 16 then become

$$\bar{\bar{\sigma}} = \frac{\rho \left(\frac{q}{m} \right) \tau}{(\omega_c \tau)^2 + (1 + i\omega\tau)^2} \begin{pmatrix} (1 + i\omega\tau) & \omega_c \tau & 0 \\ -\omega_c \tau & (1 + i\omega\tau) & 0 \\ 0 & 0 & \frac{(\omega_c \tau)^2 + (1 + i\omega\tau)^2}{1 + i\omega\tau} \end{pmatrix} \quad (17)$$

An interesting and relatively simple case occurs when the electric field is circital to the z -axis. Note that the magnetic field $\mathbf{B}$ that we have assumed in Equation 4 is not a function of time. The difficulty in allowing $\mathbf{B}$ to vary with time is that $\mathbf{E}$ and $\mathbf{B}$ are no longer independent functions if $d\mathbf{B}/dt$ is finite. This results in more extensive mathematical analysis in finding solutions to Equation 4. The simplest possible alternative is to keep $\mathbf{B}$ constant and assume the presence of an electric field with constant magnitude $\mathbf{E}_\phi$ circital to the z -axis. One can consider $\mathbf{E}_\phi$ as either an induced electric field derived from a time-varying external magnetic field additional to $\mathbf{B}$ but applied in the same direction as $\mathbf{B}$, or an endogenous electric field connected to the presumed membrane helicity. In this regard, note that $\sigma_{11} = \sigma_{22}$ and $\sigma_{12} = -\sigma_{21}$ in Equation 17. This allows one to directly transform this tensor into either a cylindrical or a rotating coordinate system, with no changes in the elements. The result suggests that the circital current density in a plane perpendicular to the static magnetic field B_o will be governed by the expression

$$J_\phi = \sigma_\phi E_\phi \quad (18)$$

where

$$\sigma_\phi = \sigma_o \left(\frac{1 + i(\omega_c + \omega)\tau}{1 + (\omega_c^2 - \omega^2)\tau^2 + 2i\omega\tau} \right) \quad (19)$$

and

$$\sigma_o = \rho \left(\frac{q}{m} \right) \tau \quad (20)$$

The expression for the circuital conductivity, σ_ϕ , can be separated into real and imaginary parts

$$Re(\sigma_\phi) = \sigma_o \frac{1 + (\omega_c + \omega)^2 \tau^2}{D} \quad (21)$$

$$Im(\sigma_\phi) = \sigma_o \cdot Re(\sigma_\phi) \cdot (\omega_c - \omega) \tau \quad (22)$$

where

$$D = 1 + [(\omega_c^2 - \omega^2)\tau^2]^2 + 4\omega^2\tau^2 \quad (23)$$

We see that Equation 21 for the conductivity has the form of a classical resonance expression. When the frequency ω approaches ω_c , the conductivity tends toward σ_o , that level based merely upon charge carrier mobility in a uniform electric field. We further see from Equation 21 that if the mean time between collisions is much smaller than the time for one oscillation of the ion in its path ($\omega\tau \ll 1$), then the conductivity does not exhibit cyclotron resonance. Only when $\omega\tau \geq 1$ will the conductivity behave in a resonant manner. Under this condition, therefore, it is not unreasonable to suggest that for ions moving through membranes in helical paths, the conductivity will vary in a resonant way, similar to Equation 21.

APPLICATION TO Ca-EFFLUX PUBLISHED DATA

To proceed further, it is necessary to estimate a value for τ , the mean time between collisions. The real part of the conductivity (Equation 21) displays a resonance shape with a peak at $\omega = \omega_c$ and a shape factor that is governed by τ . The resonance behavior of this function can be used to advantage in comparing the results on frequency-dependent Ca^{2+} -45 efflux first reported by Bawin et al. [1975]. In this well-known experiment a clear resonance-like variation in efflux was obtained as a function of a low-frequency signal modulating a 147-MHz carrier applied to chick brain preparation. Their data indicated a peak response occurring at about 16 Hz. If one assumes a not unreasonable value for the earth's magnetic field of about 0.4 G, the ion whose cyclotron resonance is closest to 16 Hz is singly ionized potassium (K^+). Accordingly, using the charge-to-mass ratio for K^+ , we used a computer graphics program to vary B_o and τ to obtain the best fit between Equation 21 and the Bawin et al. data. The results that we obtain are

$$B_o = 0.35 \text{ G}$$

$$\tau = 0.023 \text{ s}$$

$$\sigma_o = 0.2 \text{ S/m}$$

Figure 2 shows a plot of the Bawin et al. data along with $Re(\sigma_\phi)$ as a function of frequency for several values of τ . The reader is cautioned that this value for τ is only an estimate, and that several assumptions have been made to enable us to fit the data. Although we hypothesize that a cyclotron resonance mechanism was responsible for the efflux frequency variation observed by Bawin et al. [1975], there is no way of knowing precisely whether this variation can be represented by a function having the form $\kappa\sigma$, where κ is a scaling constant. On the other hand, the rate at which work is done on the ions in our model is directly proportional to σ , and therefore the technique used in Figure 3 to estimate τ is not altogether unreasonable. Note that in Equation 21, the conductivity is given by σ_o times a shape factor. That is, the σ_o factor determines the peak conductivity, while the remainder determines both the resonance frequency and the resonance width. Whereas changing B_o (or q/m) will merely shift the resonance frequency, the resonance width is proportional to τ .

By varying the parameters that determine ω_c (B_o and q/m) we can obtain alternate sets of resonance curves. Thus, in Figure 3 we show the comparison among the ionic carriers K^+ , Ca^{2+} , and Mg^{2+} , all for the same collision time τ (.0235 s). Note that there is no way to predict the value of τ for any given carrier without first obtaining the shape of the resonance variation, as we have done above.

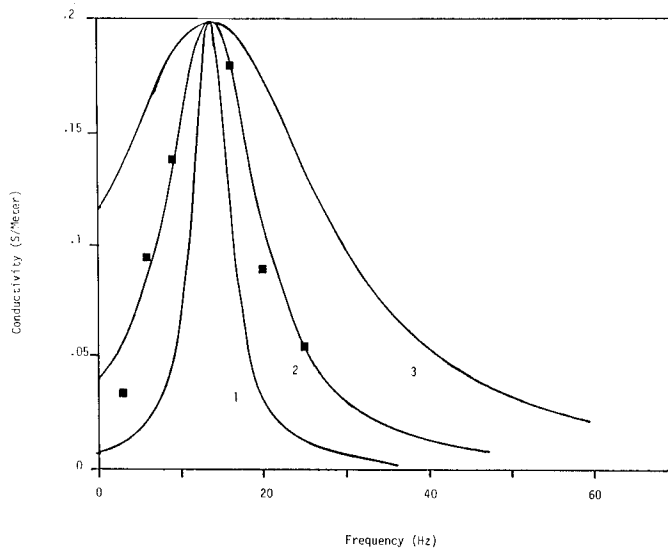


Fig. 2. The conductivity function, Equation 21, plotted against frequency for several values of the collision time τ : .01 (1), .0235 (2), and .06 (3), respectively. The charge-to-mass ratio for the potassium ion K^+ has been used, as well as a dc magnetic field $B_o = 0.35 \text{ G}$ and a dc conductivity $\sigma_o = 0.2 \text{ S/m}$. The Ca^{2+} -45 efflux data reported by Bawin et al. [1975] are also plotted. The best fit for these data occurs at $\tau = 0.0235 \text{ s}$.

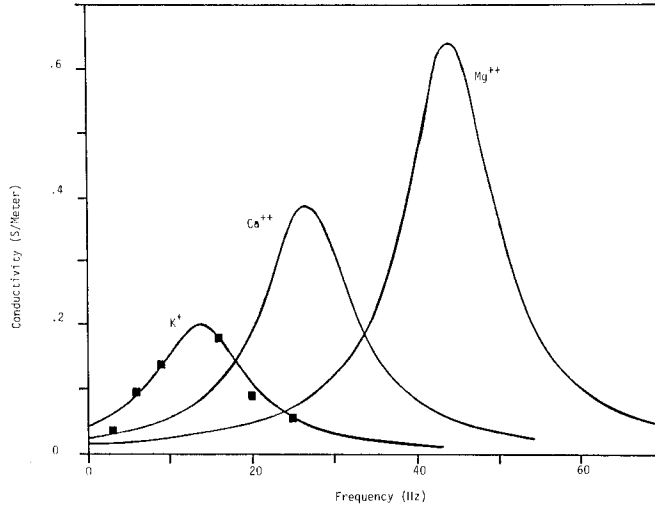


Fig. 3. The conductivity function, Equation 21, plotted against frequency for the three ions— K^+ , Ca^{2+} , and Mg^{2+} —assuming the same collision time for each ($\tau = .0235$ s). Again, the Bawin et al. [1975] data are indicated. The values of B_0 and σ_0 are the same as in Figure 2, so that the only differences in the three curves are the charge-to-mass ratios q/m .

ENERGY CALCULATION

The kinetic energy of a given ion can be estimated directly from its velocity $|\mathbf{u}|$. Combining Equations 6 and 14

$$\mathbf{u} = \frac{1}{\rho} \sigma \mathbf{E} \quad (24)$$

If $\mathbf{u}^*$ is the complex conjugate of $\mathbf{u}$, the energy W is then

$$W = \frac{1}{2} m \mathbf{u} \cdot \mathbf{u}^* \quad (25)$$

For the particular case chosen above, where

$$\bar{\sigma} = \sigma_0 \begin{pmatrix} \sigma_{11} & \sigma_{12} & 0 \\ -\sigma_{12} & \sigma_{11} & 0 \\ 0 & 0 & \sigma_{33} \end{pmatrix} \quad (26)$$

it can be shown that Equation 25 becomes

$$W = \frac{(qE_\phi)^2}{2m} \tau^2 \left[\frac{1 + (\omega_c^2 + \omega^2)\tau^2}{D} \right] \quad (27)$$

where D is defined in Equation 23. Note that for the lossless case, where $\tau \rightarrow \infty$

$$W_{\tau \rightarrow \infty} \rightarrow \frac{(qE_\phi)^2}{2m} \frac{\omega_c^2 + \omega^2}{(\omega_c^2 - \omega^2)^2} \quad (28)$$

Finally, we use Equation 27 to estimate the kinetic energy of the potassium ion, 3.45 eV. This value is calculated under the conditions $B_o = 0.35$ G, $\tau = 0.023$ s, and $E_\phi = 0.1$ V/m, at resonance. This calculation is very sensitive to the damping time τ ; a 10-fold factor in τ results in a change of 100 in the energy. Presumably the damping will be different for different ions.

MAGNETICALLY DERIVED EIGENFREQUENCIES

Perhaps the most interesting consequence of this model is the prediction of a well-defined set of gyrofrequencies, not merely one frequency, corresponding to a given ionic species and magnetic field. In other words, the fundamental frequency, as given in Equation 1, will be augmented by higher harmonics. The values of these overtones are directly related to the helical constraints within the channel. Consider Figure 1B once again. If the ionic motion along the inner periodic potential is such that a time T_o is required to traverse one wavelength, and if resonance conditions apply, then in this same period it is also possible to travel 2, 3, . . . , n wavelengths, but not any intermediate lengths. One can connect this to the channel structure by merely taking each successive wavelength traveled as one additional circuitual loop around the channel helix. This, in turn, is equivalent to saying that increasing n by one corresponds to moving the ion along the channel axis by a length equal to the pitch of the helix. This implies that n has a well-defined maximum value. It must cut off at the integral ratio given by the length L of the channel divided by the pitch p . The allowed frequencies are $1 \cdot 2\pi/T_o$, $2 \cdot 2\pi/T_o$, $3 \cdot 2\pi/T_o$, . . . , $n \cdot 2\pi/T_o$, which can be conveniently expressed as

$$\omega_n = n\omega_c \quad (n = 1, 2, 3, \dots, L/p) \quad (29)$$

where

$$\omega_c = 2\pi\nu_c = \frac{2\pi}{T_o} \quad (30)$$

The theory that we have developed above leads to the interesting possibility that the conductivity in a channel is quantized in the presence of a magnetic field. We obtain, from Equation 29

$$\sigma_n = n\sigma_o \quad (n = 1, 2, \dots, L/p) \quad (31)$$

where σ_o , defined in Equation 20, is rewritten according to Equation 1

$$\sigma_o = \rho \left(\frac{\omega_c \tau}{B_o} \right) \quad (32)$$

(The relation between the channel characteristics and the conductivity is shown in

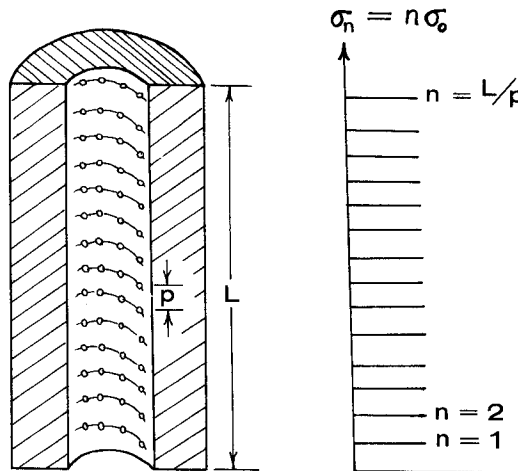


Fig. 4. Suggested connection between channel structure and conductivity states. Transiting ions are constrained to a transport velocity related to the helical pitch p of the channel lattice. Because of the intrinsic periodicity within the lattice, there will be additional modes of motion corresponding to multiples of p , and therefore to a set of multiple conductivities σ_n , equal to an integer times a ground-state conductivity σ_0 . There are two interesting consequences: the conductivity will appear to be quantized in units of σ_0 , and the largest value that the integer n can take will be determined by the length L of the channel over which this periodicity is maintained, such that $n_{\max} = L/p$.

Figure 4). One finds a set of quantized states for the conductivity, derived directly from the cyclotron resonance eigenfrequencies.

There is some experimental evidence in support of this prediction. A number of recent reports [Hamill and Sakmann, 1981; Geletyuk and Kazachenko, 1985; Krouse et al., 1986] have observed multiple conductance states in single channels using patch-clamp techniques. Specifically, in these experiments a set of conductance substates is measured such that the states are restricted to integral values of some fundamental level σ_0 . To the best of our knowledge, there has been no adequate explanation for this effect in terms of an existing channel model. Note particularly that the maximum number of states in a single channel that has been measured to date in a multiple conductance channel is $n = 15$ [Geletyuk and Kazachenko, 1985]. This is in reasonable agreement with what we suggest, if one assumes a channel having an overall length of 60 Å and a helical pitch of about 4 Å. Additional evidence in support of such eigenfrequencies is found in recent work by Blackman et al. [1985b]; in following up their original work [Blackman et al., 1985a] they found two sets of frequencies that were effective in enhancing calcium efflux. In the lower set, there were five frequencies, ranging from 15 to 135 Hz. Unlike the simple analysis we have provided above, the frequencies of Blackman et al. indicate a $(2n + 1)$ multiplicity. Thus, if 15 Hz is the fundamental in these experiments, only *odd* harmonics (15, 45, 75, . . . , Hz) are observed. A strikingly similar resonant behavior has also been observed [McLeod et al., 1986; Smith et al., 1987] in the calcium-dependent motility of marine diatoms. The lack of *even* harmonics in such resonance experiments is a fascinating puzzle. Nevertheless, there is now experimental evidence for the existence of eigenfrequencies in membrane transport processes.

DISCUSSION

The consideration of damping loss stemming from Equation 3 has a number of consequences. The cyclotron resonance model can now be tested against calcium

efflux experiments, as shown in Figure 2. In view of the fact that the original Bawin et al. [1975] results are consistent with the present model, coupled with the fact that there simply is no other quantitative explanation for their results, we believe that a cyclotron resonance mechanism was probably the basis for their observations. Although they did not report the local magnetic field at the time, one can be confident that a non-zero local field did exist near their apparatus, probably not very different from the 0.35 G we assumed in attempting to fit the shape of their frequency variation to our resonance curves. The resulting collision time, ~ 0.025 s, would not be greatly changed if another geomagnetic level were assumed, inasmuch as the resonance width that determines τ is not strongly dependent on B_0 . Long biological relaxation times, of the order of tens of milliseconds, raise interesting questions. It is difficult to find physical arguments in support of relaxation times as long as 0.01 to 0.1 s. On the other hand, it may have escaped the attention of the scientific community that the relatively sharp resonances first observed by Bawin et al. [1975] lead inescapably to the existence of such times. Adey [1981] for one was aware of this problem when he suggested the likelihood of low-noise (i.e., low collision rate) pathways for charged particles in membranes. We agree with this view, but also maintain that these low-noise pathways are restricted solely to the channel-forming proteins. It should be noted that others have reported long relaxation times in proteins. For example, Furuya et al. [1986] report well-characterized time constants of 26 ms up to 1 s reported by different observers studying relaxation time constants of bacteriorhodopsin photosignals.

It is reasonable to suggest that there will be an energy loss transmitted to the constraining walls of the channel and thus to the protein lattice. It is beyond the scope of the present work to pursue these details; quantum-mechanical calculations probably will be required to study excitations in the channel lattice. However, it seems clear that in order to sustain the ionic eigenfrequencies we have been discussing, the lattice vibrations must be matched to, or nearly in phase with, the transiting ion. One way of interpreting the damping constant b in Equation 3 is as a measure of the mismatch between the longitudinal or torsional oscillations of the lattice and the cyclotron resonance frequency.

A separate, but connected, question relates to the source of the kinetic energy that is supplied to the ion. It was suggested [Liboff, 1985] that the energy density of the oscillating electric or magnetic field itself might be converted in a resonance condition, but a simple calculation shows conclusively that the kinetic energy we estimate using Equation 28 is much larger than can be derived from field conversion directly. The frequencies are sufficiently small that we can assume that quasistatic conditions apply. Then the energy density in a low-frequency magnetic field, say at $B_{\text{rms}} = 0.25$ G, is about 1.5×10^{15} eV/m³. If we assume that a single cell has a volume ~ 125 μm^3 , this implies that the maximum energy available to an *entire* cell, if such energy conversion were indeed possible, would be no more than ~ 0.2 eV.

By contrast the volume of a single channel is down by a factor of more than 10^9 from that of a cell, and therefore there simply is not enough magnetic energy content in a single channel to warrant consideration of such direct magnetic energy conversion. Furthermore, comparison of the relative energy densities in quasistatically varying E and B fields for the sort of levels we are considering (0.1–1 G, 0.1–1.0 V/m) indicates that such electric fields carry even less energy density than magnetic fields.

One can speculate that the low-frequency electromagnetic field somehow couples to the lipid surface, possibly through the counter-ion charge sheet [Grotsky, 1975], providing acoustic modes in the cell membrane that reappear within the

channel proteins as cyclotron resonance modes. One may also suggest a connection to the free energy release resulting from the hydrolysis of adenosine triphosphate (ATP). The 0.42 eV provided in this reaction couples to the protein in an unknown way. Davydov and Kislukha [1973] proposed a mechanism whereby this energy is trapped in the lattice through an interaction with low-frequency longitudinal acoustic phonons and propagates through the protein as a soliton. Lawrence and Adey [1982] extended this approach to excitable tissue. Despite the fact that Lomdahl and Kerr [1985] calculate that the random displacements produced by thermal motions in the protein at biologically relevant temperatures are much larger than the displacements needed to take advantage of acoustic phonons, they nevertheless state that "the α -helix structure is complex enough to provide other candidates for coupling." The protein lattice probably plays a key role in ionic transport through channels, as an intermediate structure capable of converting energy appearing at the membrane boundaries to ionic kinetic energy. One can conceive of the energy transfer to the ion taking place via a set of normal modes of vibration in the lattice, equivalent to a degenerate set of eigenstates in which the degeneracy is removed by application of a local magnetic field in cyclotron resonance with the system. As was already pointed out, the ion-lattice coupling is expected to be less than perfect, so that damping losses will broaden each of the resonant frequencies.

In a separate approach aimed at explaining the interaction mechanism between ELF magnetic fields and cellular systems, Chiabrera et al. [1985] have shown that Lorentz forces on charged ligands near surface receptors may result in resonant changes in ligand drift velocity, thereby affecting surface attachment and ion transport. As in the channel model we have developed here, the question of collision time is also critical to the ligand surface receptor model. Placing the interaction at the channel instead of the membrane surface has two great advantages: 1) the periodic nature of the channel structure leads directly to the possibility of eigenfrequencies and 2) if the interior of the channel is aqueous [Skerra and Brickmann, 1987], one does not have to account for the energy of hydration of an ion as it leaves the solution.

In conclusion, the cyclotron resonance mechanism for ion transport through membrane channels appears to be helpful in explaining a wide variety of puzzling results in different experiments; not only does it predict the observed fundamental frequencies in calcium-efflux experiments, but it also predicts the existence of additional harmonic frequencies in these experiments and serves to provide a relatively clean explanation for the multiple conductance states in membrane channel experiments. Using this model, it is possible to obtain reasonable estimates for both the energy of a given ion at resonance and the approximate overall number of frequency modes. On the negative side, we have yet to explain the forbiddenness of even modes which has been observed recently in two separate laboratories. Nevertheless, it seems rather clear that the present approach serves to rationalize an area of research that has heretofore been studied solely in a phenomenological manner.

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